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(54) Multi-well filter strip and composite assemblies.

(57) A filter strip (18) and composite assemblies for filtering microliter quantities of fluids. A linear array of wells (20) having open top (22) and bottom (24) ends are connected by frangible webs in spaced-apart relation with discrete filter membranes closing the bottom (24) ends of each well (20). Tabs (30,32) are provided on the ends of the filter strip for holding the same and supporting the strip in a rectangular holder (170) having alpha-numeric designations for identifying each well (20) in a plurality of such filter strips contained within the holder (170). The filter strip may be used in a vacuum manifold for applying a pressure differential across the filter membrane and directing the filtrate into an aligned aperture of a closed bottom well of an array of wells held within the manifold. Alternatively, the filter strip may be used with a transfer plate for directing the filtrate from each well (20) of the filter strip to an aligned well of a closed bottom array of wells. Another composite assembly includes a pressure manifold for applying an increased pressure above the membranes.

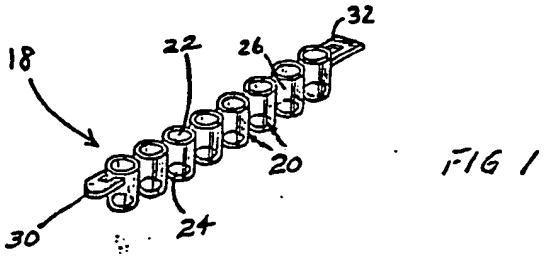

FIG 1

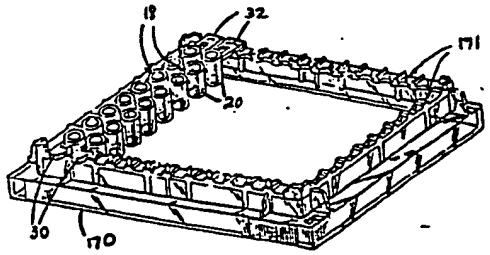

Fig. 9

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filter strip, transfer plate, and multi-well test plate wherein the transfer plate directs the filtrate passing through the membrane into a corresponding well of the test plate.

Summary of the Invention

The invention is a multi-well filter strip and composite assemblies for filtering small quantities of liquid.

The filter strip consists of a plurality of cylindrical wells open at the top and bottom ends and arranged in a straight row and connected to one another by frangible webs which space the wells closely adjacent one another, but not touching, and discrete filter membranes closing the bottom end of each well with the filter membranes spaced from one another. The filter strip has outwardly extending tabs at each end for holding the strip and supporting the strip in a rectangular frame having an array of alpha-numeric designations for identifying each well supported by the holder. The strips are releasably attachable to the holder and the wells within each strip are releasably attached to permit separation of any number of wells in the strip.

A filter assembly includes a vacuum manifold having a base and removable cover, a chamber in the vacuum manifold, a passage in the manifold communicating with the chamber for applying a reduced pressure to the chamber, a multi-well filter strip, an array of cylindrical recesses in the cover for supporting the filter strip, and openings in the bottoms of the recesses for placing each membrane of the filter strip wells in communication with the chamber whereby a reduced pressure applied to the chamber will draw liquid in the wells through the membranes into the chamber. A closed bottom well strip may be positioned in a trough in the manifold base with each well of the array aligned below a well of the filter strip where it is desired to separately collect the filtrate passing through each membrane of the filter strip. A nozzle is provided around each opening in the cover for directing the filtrate from the membrane into an aligned closed bottom well for preventing spattering and cross contamination of the filtrate. The cylindrical recesses in the manifold cover for supporting each well of the filter strip each have a central funnel-shaped portion and a peripheral shoulder for supporting the periphery of the membrane and forming a seal at the bottom of the well. A vacuum control device is provided in the manifold cover for limiting the reduced pressure applied to the chamber. A fan-shaped passage is provided in the base of the manifold for removing the filtrate drawn into the chamber which is not contained within the closed well strip.

In another embodiment, a filter assembly is provided consisting of a multi-well filter strip, an array of closed bottom wells similar in size to the filter strip and disposed beneath the filter strip, and a transfer plate between the filter strip and closed bottom well array for engaging and aligning the same and causing the filtrate passing through each membrane of the filter strip to enter a corresponding separate well in the array. The transfer plate may be utilized in a pressure manifold for applying an increased pressure above the membranes of the filter strip to force liquid through the membranes.

Brief Description of the Drawings

Fig. 1 is a perspective view of a filter strip constructed in accordance with this invention.

Fig. 2 is a side view of one well of the filter strip of Fig. 1, showing in cross-section the web which connects adjacent wells.

Fig. 3 is a cross-sectional view of the filter strip of Fig. 1.

Fig. 4 is a cross-sectional view of an assembly composed of a vacuum manifold having a base and cover, a closed well plate in the base, and a filter strip mounted on the manifold cover in accordance with this invention.

Fig. 5 is a top perspective view of the manifold base of Fig. 4.

Fig. 6 is a cross-sectional view of a vacuum manifold similar to Fig. 4 but having a device for controlling the amount of vacuum.

Fig. 7 is a fragmentary cross-sectional view of the well chambers in the manifold covers of Figs. 4 and 6.

Fig. 8 is a fragmentary cross-sectional view of an assembly composed of a filter strip, strip holder, centrifugal transfer plate, and closed well plate in accordance with the present invention.

Fig. 9 is a top perspective view of a strip holder containing two filter strips as used in the assembly of Fig. 8.

Fig. 10 is a top plan view of the centrifugal transfer plate as used in the assembly of Fig. 8.

Fig. 11 is a side plan view of the transfer plate of Fig. 10.

Fig. 12 is a fragmentary cross-sectional view of the transfer plate taken along section lines 12-12 in Fig. 10.

Fig. 13 is a fragmentary cross-sectional view of the transfer plate taken along section lines 13-13 in Fig. 10.

Fig. 14 is a cross-sectional view of an assembly composed of a pressure manifold, a rubber gasket, a filter strip, a transfer plate and a closed well plate, in accordance with the present invention.

cover, liquid may be pulled from the wells of the filter strip through the membranes 34 when a pressure differential is applied across the membranes (i.e., by reducing the pressure in chamber 70). The filtrate pulled through the membranes may be either individually collected in the wells of the closed bottom well strip 76, or it may be mixed in the chamber 70. This latter arrangement would typically be used when the object is to collect the retentate in the filter strip wells rather than the filtrate from them. When the filtrate is the product to be derived from the procedure, obviously, separate wells 78 must be provided to collect the fluid separately from each of the filter strip wells 20.

The trough 74 formed in the base 62 of the vacuum manifold 60 serves to align the individual closed bottom wells 78 of the array 76 with the wells 20 in the filter strip 18. As is evident in Fig. 4, the opening 92 through the bottom wall 86 of each recess in the cover is aligned with the approximate center of the corresponding closed bottom well 78 when positioned in the trough 74 so that all of the filtrate is collected in the corresponding closed bottom well 78. To further assure discharge of the filtrate into the closed bottom wells, a downwardly extending flange 94 may be provided in the cover about each of the openings 92. Each flange 94 about its opening 92 defines a nozzle so as prevent the filtrate from spattering as it exits the passage 92 particularly if high vacuum (i.e., very low pressure) is applied to the chamber 70 causing high flow rates.

In Fig. 6, one of a variety of different devices which may be used to limit the vacuum applied to chamber 70 is shown incorporated into the vacuum manifold 60. In that figure, a duckbill valve 100 is shown formed in the cover 64 at one end of the row of wells 80. Alternatively, a ball check valve or any other well-known pressure relief device may be provided. Any of those arrangements will prevent excessive vacuums from being applied to the chamber 70, which would cause spattering or exceed the pressure which can be withstood by the membranes 34 that form the filter material across the bottoms of the wells 20. More preferably, the valve 100 is provided adjacent the passage 110 described below for even pressure control across the filter strip.

The means for applying a vacuum to the chamber 70 is shown in Fig. 5. A passage 110 extends through the side wall 112 of trough 74 and through a nipple 114 onto which tubing may be telescoped so as to connect the passage 110 to a vacuum pump (not shown). The opening 110 in this embodiment is shown to be generally fan-shaped, and its cross-sectional area diminishes smoothly from the inner surface 116 of trough side wall 112 to the extension of the passage 110 in nipple 114. The bottom of passage 110 in side wall 112 is at or below the level of the bottom wall 118 of the trough so that any liquid in the trough may be drawn by the vacuum out of the manifold through nipple 114. The fan-shaped arrangement of opening 110 disperses the airflow across substantially the entire bottom wall 118 of trough 74 so as to avoid spattering of any filtrate in the trough. It will be appreciated that if closed bottom wells are not provided in the trough, but rather the filtrate is permitted to collect in the trough itself, the configuration of the passage 110 will facilitate removal of all of that material. It is important that the passage 110 through which the vacuum is applied to the chamber 70 be in a position to remove all of the liquid which collects in the chamber.

In Figs. 8-13, another assembly employing the filter strips is shown. In this assembly, shown in Fig. 8, a centrifugal transfer plate 120 places one or more filter strips 18 in communication with the closed bottom wells of a conventional 96-well plate 122 and transfer of the filtrate from the wells of strips 18 to the wells of plate 122 is induced by the action of a centrifuge (not shown). As shown in Fig. 9, a plurality of filter strips 18 are supported by a strip holder 170, which holder is described in detail in copending application Serial No. 923,906. Holder 170 engages the peripheral edge of well plate 122 as described hereinafter. While a 96-well plate 122 is suggested, it should be appreciated that the plate may be replaced by a number of closed bottom strips identical to those shown in copending application Serial No. 923,906, which may in turn be supported by a strip holder as shown in that application. The two holders for the filter strips and closed well strips may then register with one another in a manner similar to that shown in Fig. 8.

The transfer plate 120, shown separately in Figs. 10-13, is a molded plastic piece having a number of cylindrical recesses 130 formed in its upper surface 144. Recesses 130 have vertical sidewalls 131 surrounding horizontal shoulders 132, which surround funnel-shaped bottom walls 133. Bottom walls 133 register with downwardly extending nozzles 134 having openings 136 therethrough. Each of the nozzles 134 has an outer diameter which enables it to register with the open top 138 of a well 140 in the 96-well plate 122 (see Fig. 8). The fit of the nozzle 134 in the open well 140 is such that a slight clearance is provided through which any build up of gas in the well 140 may be vented. The nozzles 134 extend downwardly from the lower surface 142 of the transfer plate so as to enter into the closed bottom wells 140 and prevent cross contamination of filtrate from one well to another in plate 122.

The vertical walls 131 of recesses 130 engage the outer sidewalls of wells 20 of filter strip 18

the user. Waste is reduced by enabling the user to select only the number of strips required.

It will also be appreciated that a filter as a substrate base is very desirable in many analytical diagnostic applications where the test being performed relies upon the physical or chemical binding of the test sample to the internal and external surfaces of the substrate. A microporous membrane has a vastly greater surface area than a nonporous flat surface, and therefore a very substantial increase in binding occurs. Furthermore, many specialized membrane materials, including ultrafiltration media, are available to achieve specific binding properties (as used herein, filter membrane includes ultrafiltration media). It will also be appreciated that after the binding steps are complete, most diagnostic tests reguire a series of reaction and washing steps to flush away the unreacted or unbound material. The use of an eight-well strip with either a vacuum manifold or centrifugal transfer plate enhances the ease with which the reaction and washing steps may occur.

As a further advantage of this invention, during an incubation period the well tops of the filter strip can be sealed with a plate or stopper (e.g., a pressure sensitive film) and the filter strip placed over a closed bottom strip in which water has been added to maintain the humidity and prevent dehydration. The lower strip also prevents the contents of the filter strip from dripping onto the workbench.

Having described this invention in detail, those skilled in the art will appreciate that numerous modifications may be made thereof without departing from its spirit. Therefore, the breadth of this invention is not to be limited to the specific embodiments illustrated and described. Rather, its breadth is to be determined by the appended claims and their equivalents.

Claims

1. A filter strip comprising
a plurality of generally cylindrical wells open at their top and bottom ends and arranged in a straight row with their axes parallel to one another and connected by frangible webs which space the wells closely adjacent one another, but not touching, and
discrete filter membranes closing the bottom end of each well with the filter membranes spaced from one another.

2. A filter strip as defined in claim 1 wherein outwardly extending tabs are secured to the end wells of the strips for supporting the strip.

3. A filter strip as defined in claim 1 wherein the bottom ends of the wells and the filter membranes all lie in the same plane.

4. A filter assembly comprising
a vacuum manifold having a base and removable cover,
a chamber in the vacuum manifold,
a passage in the manifold communicating with the chamber for applying a reduced pressure to the chamber,
a multi-well filter strip having filter membranes closing the bottom of each well of the strip,
means provided on the outside of the cover for supporting the strip, and
openings in the cover for placing each membrane in communication with the chamber whereby a reduced pressure applied to the chamber will draw liquid in the wells through the membranes into the chamber.

5. A filter assembly as defined in claim 4 wherein
the means provided on the cover comprises a plurality of individual recesses in the outer surface each receiving the bottom end of one well of the filter strip, and
said openings in the cover extend from the bottom of each recess into the chamber.

6. A filter assembly as defined in claim 4 wherein
the means provided in the cover prevents the intermixing of filtrate passing from each well through the membrane to the chamber.

7. A filter assembly as defined in claim 6 wherein
means is provided in the chamber for supporting a second multi-well strip whereby each well in the second strip receives the filtrate from a separate well in the filter strip.

8. A filter assembly as defined in claim 5 wherein
each of the recesses has a bottom wall funnel-shaped at its central portion and surrounded by a flat shoulder,
the flat shoulder of each recess forming a seal with the bottom of each well when the multi-well filter strip is mounted with its wells in the recesses.

9. A filter assembly as defined in claim 8 wherein
the openings in the cover communicate with the lowermost point of the funnel-shaped portions of the bottom walls of the recesses.

10. A filter assembly as defined in claim 6 wherein
outwardly extending tabs are secured to the end wells of the strips for supporting the strip.

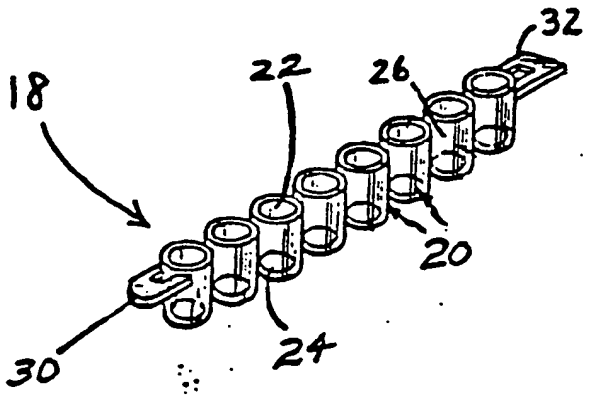


FIG 1

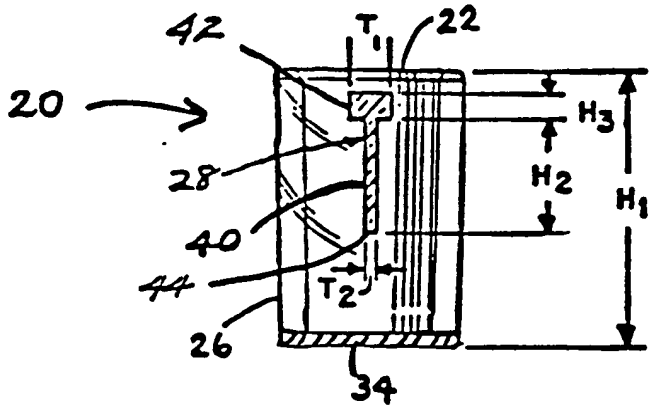


FIG 2

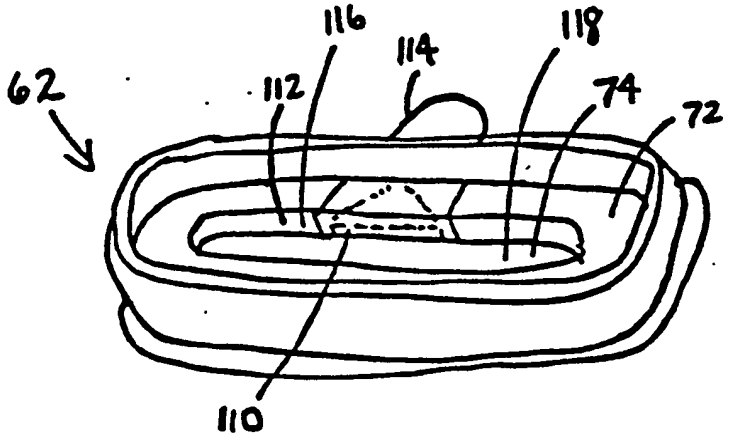
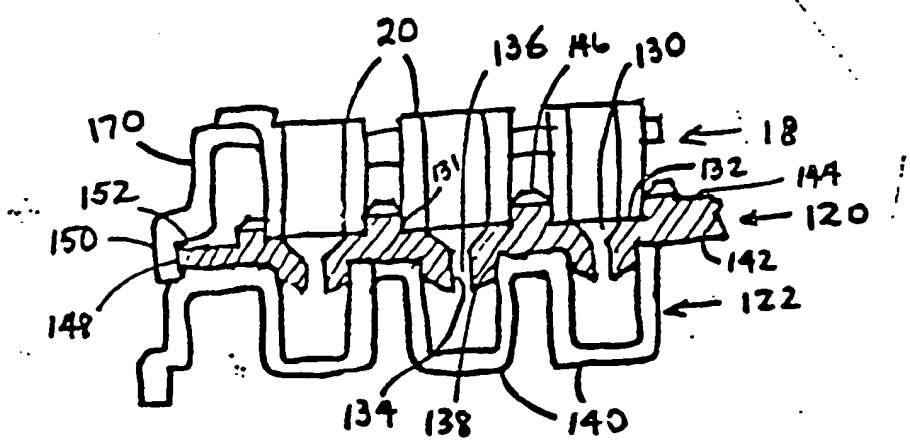


FIG 5


20
136
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170
18
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122
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140

Fig. 8

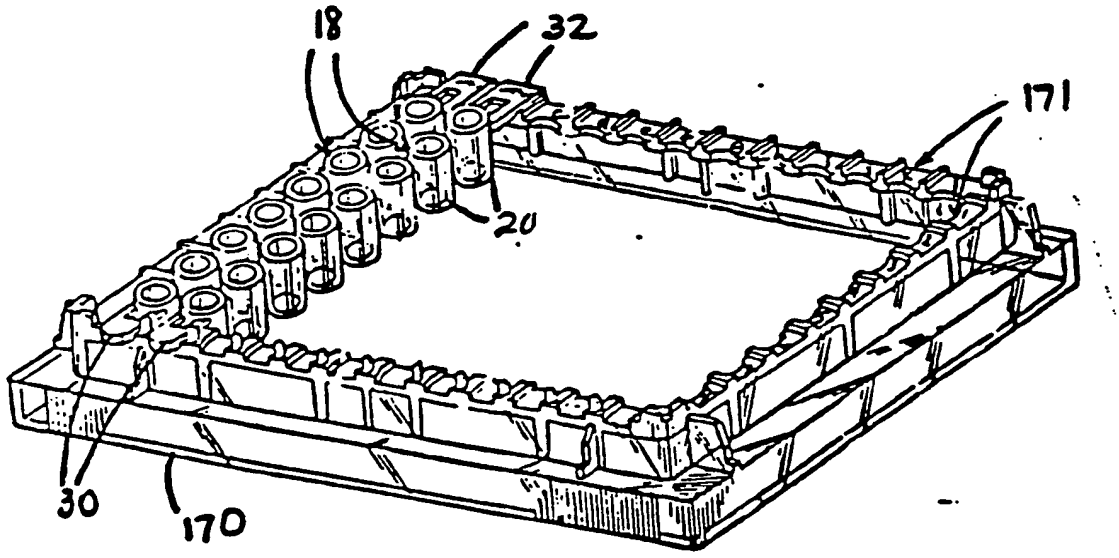
18
32
171
20
30
170

Fig. 9

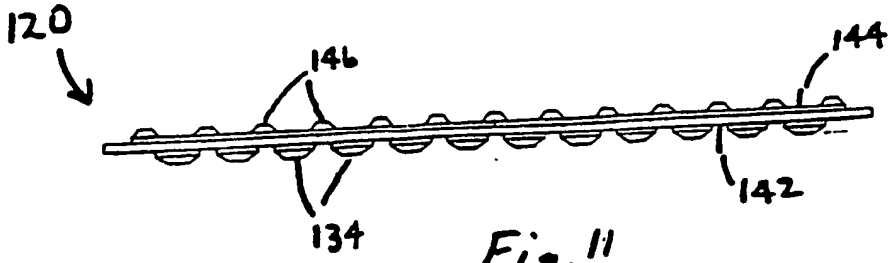

Fig. 11

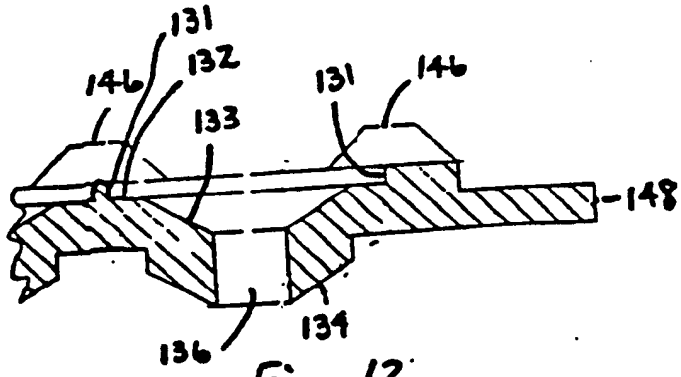

Fig. 12

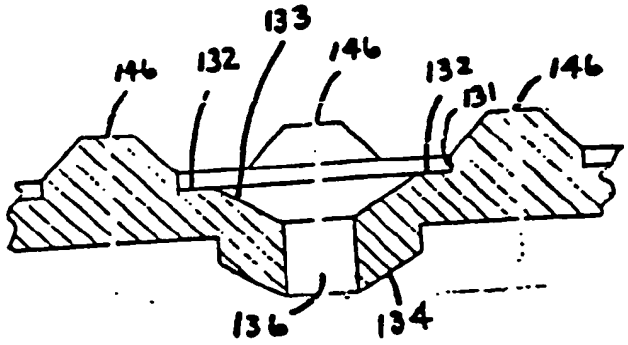

Fig. 13

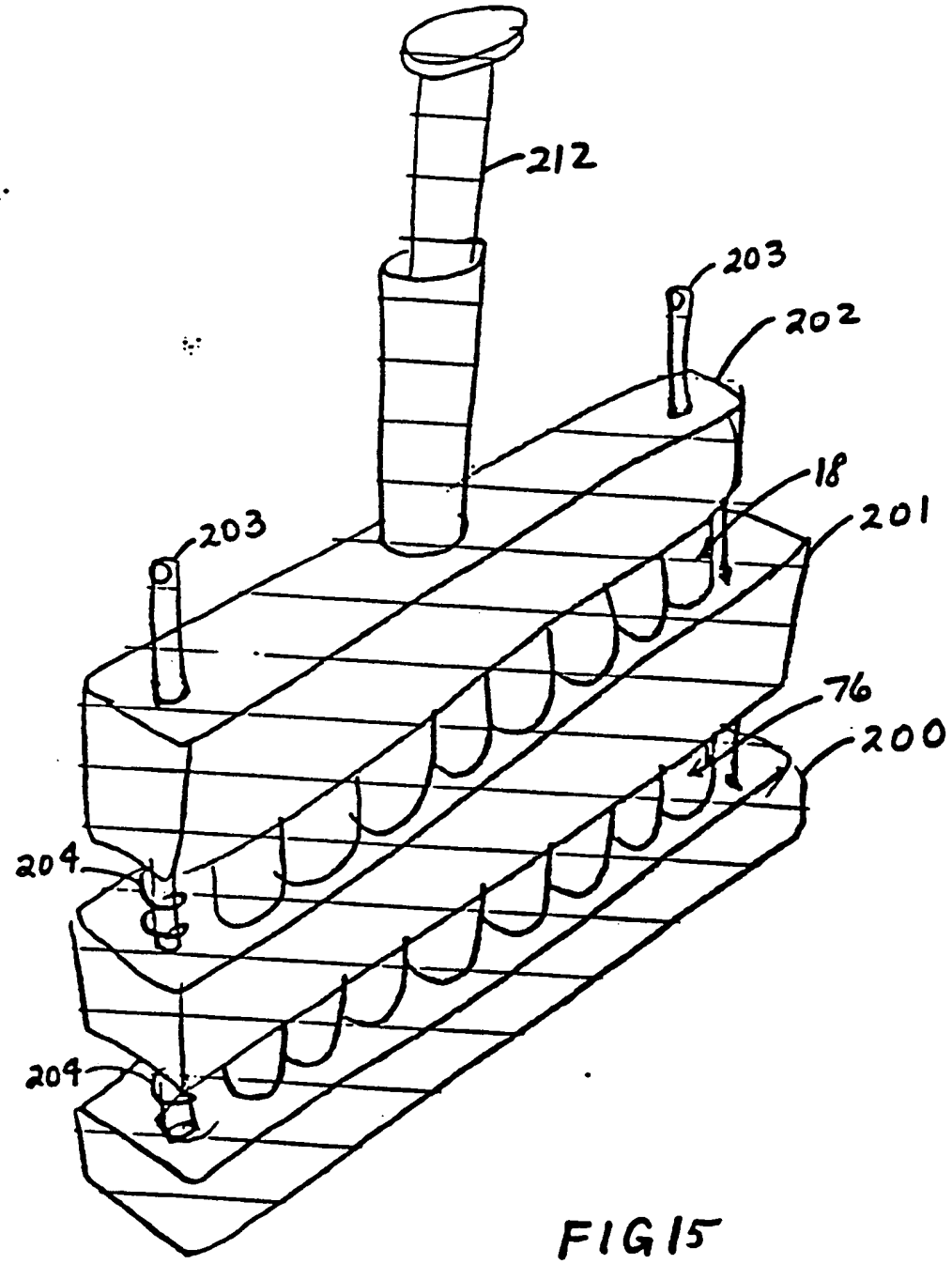

FIG 15